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Seasonal modifications in blood pressure are mainly related to interdialytic body weight gain in dialysis patients

ÀNGEL ARGILÉS, RONAN LORHO, MARIE-FRANÇOISE SERVEL, GUILLAUME CHONG, PETER G. KERR, and GEORGES MOURAD

Laboratoire de Génomique Fonctionelle-CNRS UPR 2580; Department of Nephrology, University Hospital Lapeyronie; Néphrologie-Dialyse St. Guilhem (NDSG); Association pour l'Installation à Domicile des Epurations Rénales (AIDER), Montpellier, France; and Department of Nephrology, Monash Medical Centre, Clayton, Victoria, Australia

Seasonal modifications in blood pressure are mainly related to interdialytic body weight gain in dialysis patients.

Background. Longitudinal studies in dialysis patients have identified seasonal variations in blood pressure that may follow climatic parameters such as external temperature and humidity. We aimed to assess the participation of interdialytic body weight gain variations in the seasonal profile of blood pressure.

Methods. Ninety-nine stable patients (40 F/59 M), 52.9 ± 1.5 years old, dialyzed in a single satellite dialysis unit between January 7, 1991, and September 30, 1998 were studied. Supine systolic and diastolic blood pressure, body weight, and interdialytic body weight gain were determined at every one of the 38,769 dialyses included, and studied along with climatology data obtained from Météo, France.

Results. Blood pressure varied throughout the year, following a cyclic pattern. It increased from the autumn months toward winter, and decreased toward the spring and warmer months. Systolic and diastolic blood pressures were strongly correlated with interdialytic body weight gain ($r = 0.925$; $P < 0.0001$ and $r = 0.888$; $P = 0.0001$, respectively). Blood pressure was also correlated with the climatic factors: rainfall ($r = 0.786$; $P < 0.003$ and $r = 0.784$; $P < 0.003$), humidity ($r = 0.701$; $P = 0.011$ and $r = 0.699$; $P < 0.012$), and day light span ($r = -0712$; $P < 0.01$, and $r = -0.658$; $P < 0.02$, respectively). Multivariate regression analyses taking blood pressure as a dependent variable retained interdialytic body weight gain as the first variable in the model.

Conclusion. Our results establish a strong link between blood pressure variations and interdialytic body weight gain, showing the important participation of volume state in modulating blood pressure in this group of patients.

Blood pressure has been observed to vary seasonally in normal subjects [1] and in hypertensive patients [2]. It has been shown that stroke [3], chronic heart disease, and mortality [4, 5], as well as nontraumatic aortic rupture [6] also follow seasonal variations that parallel those of blood pressure, supporting a causal effect of blood pressure on the occurrence of these life-threatening cardiovascular complications [3–6].

A clear seasonal pattern in blood pressure has recently been identified in dialysis patients [7]. Because hemodialysis patients are repeatedly and regularly examined (three times a week) in a very reproducible manner, they represent a unique group of patients suitable to analyze longitudinal variations of cardiovascular status, including blood pressure and hydration levels. Accordingly, in a longitudinal study over a 4-year period, we were able to establish a link between blood pressure variations in dialysis patients and climatic factors such as external temperature and humidity [7]. Nevertheless, other causal factors, also with seasonal variations, may be at the origin of the evolution of blood pressure throughout the year. Extracellular volume variations, sun exposure [8], and dietary modifications are among the candidates that may influence blood pressure. Recently, a multicenter study from the American Hemodialysis (HEMO) trial confirmed our findings on blood pressure variations, and further identified a significant seasonality in 13 out of 21 laboratory and clinical variables analyzed [9]. However, the precise participation of these factors in the seasonal variation of blood pressure has not been elucidated. Furthermore, in a longitudinal-type study, factors linked to time (e.g., age, time-related chronic renal failure complications, comorbidity, and others) may interfere in the analysis of the seasonal cycle of blood pressure.

In the present study, in order to progress the understanding of seasonal blood pressure variations, we wanted to separate time- and age-related factors from the actual annual cycle of blood pressure. We analyzed each month without distinction of the year it belonged to, breaking the longitudinal effect of time and focusing on a 12-point study corresponding to the year cycle. From this analysis, it became apparent that interdialytic body weight

Key words: seasonal variation, blood pressure, extracorporeal circulation (dialysis patients), blood volume, climatic factors.

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Table 1. Patient descriptions

Patients (*N*)	99
Sex *F/M*	40/59
Age *years at start of dialysis*	53.1 ± 1.5
Previous dialysis treatment *months*	50.8 ± 7.2
Dialysis treatment in the unit *months*	42.6 ± 3.4
Renal disease	
Chronic GN	39
Genetic renal disease	16
Chronic interstitial nephritis	10
Diabetes	6
Nephroangiosclerosis	10
Unknown	18

gain was a determining factor in blood pressure modifications. Further, both blood pressure and interdialytic body weight gain follow a seasonal pattern that is related to rainfall and humidity.

METHODS

Dialysis facility

A single-satellite dialysis unit equipped with real-time computerized clinical records since 1991 was the center for the study. After dialysis strategy decisions, only clinically stable patients were treated in this unit, which performs an average of 450 dialysis treatments per month. Any programmed surgery or unexpected clinical event requiring in-hospital treatment motivated temporary or definitive exclusion of the patient from the unit. During the assessed period, a total of 131 patients were treated in our unit. Thirty-two of them had remained for less than 6 months and were excluded from the study. The yearly mean flow of patients was 19.8%, and the main causes for departure were transfer to other units (8.4%), transplantation (7.2%), and death (4.2%). The present study concerns the analysis of the 38,769 dialysis treatments performed between the 1st of July, 1991, and the 30th of September, 1998, in the patients who remained in the unit for more than 6 months.

The technical characteristics of this satellite unit have been described elsewhere [10]. Blood pressure was measured with automated devices (Dinamap 8103; Critikon, Creteil, France) that were regularly calibrated. Heart rate and systolic and diastolic blood pressure were measured in the supine and erect positions before every dialysis session after the patient had rested for 10 minutes, and the values were recorded. The clinical follow-up included automated measurements of blood pressure before, during, and after dialysis, and continuous measurement of weight (Gambro weigh beds; Gambro, Lund, Sweden). The patients were regularly seen during dialysis by the renal physician present full time in the unit, and dry weight was modified as frequently as needed. We base our definition of dry weight on a clinical evaluation; it is an ongoing process of re-evaluation of clinical volume status (in our practice, presence or absence of edema, satisfactory blood pressure, and a stable, normal range cardiothoracic index in the x-ray), blood pressure, and previous dry weight target, with the intention of optimizing blood pressure control without antihypertensive drugs where possible, and while avoiding the hypotensive accidents during dialysis and in the postdialysis period.

Dialysis dose was assessed monthly by per-dialytic in vivo urea clearance assessment with blood determinations of urea, bubble-measured blood pump flow, and measurement of blood access recirculation. Routine hematologic and biochemical determinations were performed monthly, including calculation of dialysis dose (Kt/V) and protein catabolic rate (PCR).

Patients

Ninety-nine patients were treated for more than 6 months in the unit during the selected period of time, including 40 females and 59 males, 53 ± 1.5 year old (range 19 to 79 years). They spent 42.6 ± 3.4 months in the unit. Their clinical characteristics are described in Table 1. Sixteen patients regularly received antihypertensive drugs (calcium antagonists, beta-adrenergic antagonists, or angiontensin-converting enzyme inhibitors).

The study was carried out in agreement with the French Laws (Code de la Santé Publique, Loi Informatique et Libertés 1978, and Loi Huriet-Sérusclat 1988), and respected the anonymity of the data included.

Climatologic data

The climatologic data were obtained from the local agency of the National weather services of France (Météo-France, Montpellier) in Montpellier (located in the south of France, adjacent to the Mediterranean sea). Temperature, humidity, and atmospheric pressure were measured 8 times daily, and rainfall was recorded daily.

Variables included and statistical analysis

The clinical variables retained for the study included systolic and diastolic blood pressure while in a supine position, as well as mean arterial pressure before dialysis, body weight before and after dialysis, and body weight gain between dialysis sessions. Climatologic data included maximal and minimal external temperature, maximal and minimal humidity, atmospheric pressure, and rainfall.

The data obtained were analyzed using the Statistical Analysis System package V8.02 (SAS Institute, Inc., Cary, NC, USA). The values of all the variables included were averaged per natural month without distinction of the year. Because the dialysis unit performs around 450 dialysis sessions per month, approximately 3000 blood

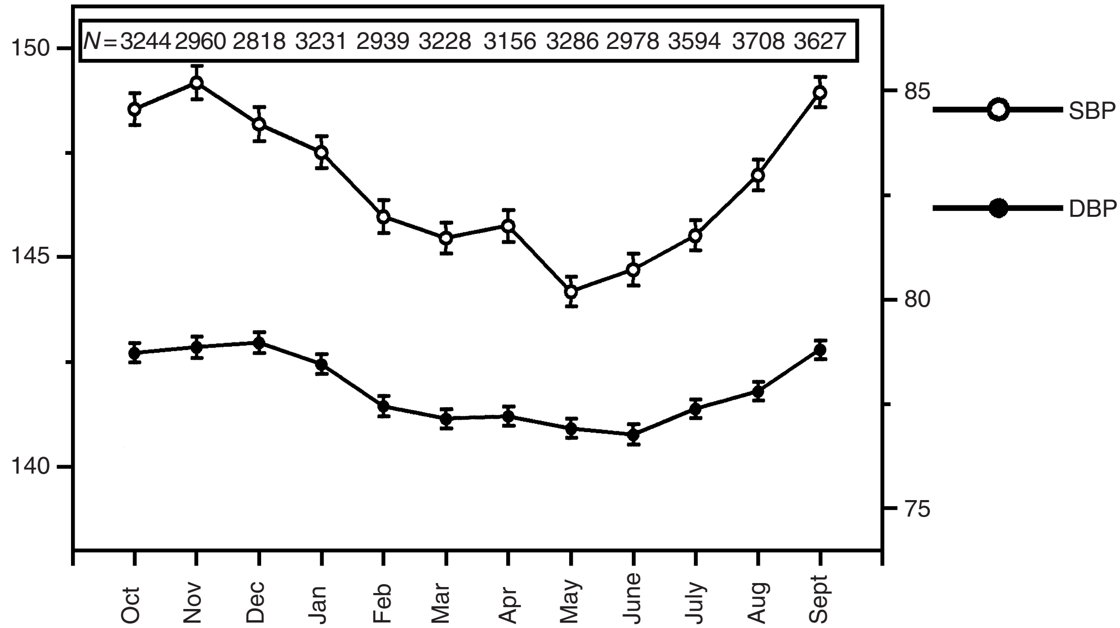

Fig. 1. Blood pressure evolution over the months of the year. The period included was from the 1st of July, 1991 to the 30th of September, 1998. The values correspond to the mean ± standard error of the mean of systolic and diastolic blood pressure of all the dialyses performed in January, February, etc., without distinction of the year of observation. The number of observations included for each data point is given. An increase in blood pressure during autumn to winter months and a decrease during spring to summer is clearly seen.

pressure and body weight measurements per natural month were averaged for the seven years included in the study. By using the average per natural month of the year, regardless of the year of measurement, we converted the longitudinal analysis in a cyclic study, with seven repeats for each month. This thereby limited the effect of confounding factors linked to the progressive increase in age, declining renal function, and urine output typically observed in dialysis patients, as well as other time-related modifications observed in renal failure.

Univariate correlations were assessed, taking into account that the patients stayed in the study for a particular length, and contributed differently to the repetitive character of the blood pressure measurements. Accordingly, and as previously described [7], Pearson's r test was assessed on the monthly values corrected after the analysis of variance. In order to avoid overestimation by the repeated character of our measurements, the observed values were corrected with a multivariate mixed model, including a random individual effect and a fixed month effect, with a covariance matrix with compound symmetry. Multivariate stepwise regression analysis was also performed, using systolic and diastolic blood pressure as the dependent variables in their respective models. The threshold for entry and stay in the model was $P < 0.15$. These analyses allowed a quantitative approach on the participation of each independent variable retained in the model for both systolic and diastolic blood pressure. Stepwise regression analysis was also used to check the influence of age, gender, and length of previous experience in dialysis before entering the study on blood pressure values. They showed that only age significantly influenced blood pressure values, confirming what is already well established.

The data are expressed as the monthly mean of the patients or climate records ± standard error of the mean. All P values are two-sided and a value of $P < 0.05$ was taken as significant.

RESULTS

The mean blood pressure of the dialyzed patients included in the study varied during the year with a sinusoid pattern. Two different parts of the curve can be easily differentiated: one with a decreasing pattern, and one with a rising pattern. Each part includes 6 consecutive values with a single exception for the smooth distribution in each cycle. The decreasing period for systolic blood pressure corresponded to the values observed from November through May, with the exception of April, which stood out of the curve. The rising part of the cycle started during May and extended through November. For diastolic blood pressure, the inflexion months were slightly shifted (December to initiate the decrease and June to initiate the increase). Therefore, considering time as a continuum, the evolution of the mean value of blood pressure during the year alternates two segments with different directions—a decreasing segment following an increasing one and vice versa (Fig. 1). The extreme values of systolic and diastolic blood pressure during the seven years

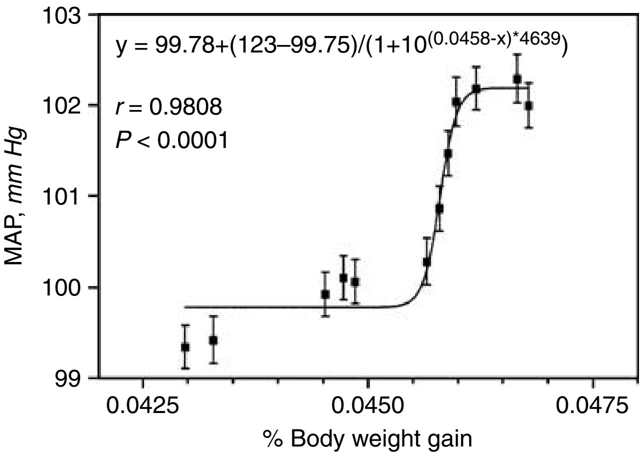

Fig. 2. Correlation study between mean mrterial pressure and extracellular fluid overload. Mean arterial pressure is significantly correlated to extracelllular volume overload, as estimated by body weight gain (see text). The distribution of the pairs has a sigmoidal shape, and the regression equation is given (the number of measurements of blood pressure included in the analysis was 38,769).

studied were 144 ± 0.36 mm Hg and 149 ± 0.40 mm Hg ($P < 0.0001$) and 76.8 ± 0.38 mm Hg and 79 ± 0.25 mm Hg ($P < 0.0001$), respectively.

We first assessed the influence of interdialytic body weight gain on blood pressure. In dialysis patients, extracellular fluid overload can be evaluated by body weight variations following fluid removal during dialysis. The theoretical normovolemic state (so-called dry weight) is obtained using a target weight for the dialysis treatment. Consequently, the volume removed during dialysis to achieve the prescribed weight, which corresponds to the body weight gain between two dialysis sessions, should be considered as fluid that the patient has in excess. Correlation analysis of the values corrected by the repetitive model (see **Methods**), showed that blood pressure was significantly correlated with body weight gain ($r = 0.925$, $r = 0.888$, and $r = 0.915$, respectively for systolic, diastolic, and mean blood pressure with $P = 0.001$ for each of them). The distribution pattern of the pairs (blood pressure/body weight gain) had a sigmoid shape. Indeed, nonlinear correlation analysis of the corrected values showed r values even greater than linear correlation studies ($r = 0.972$, $r = 0.975$, and $r = 0.9808$ for systolic, diastolic, and mean arterial pressure, respectively, $P < 0.0001$ for each of them). The regression equation for the observed values of mean arterial pressure and body weight gain in percentage is depicted in Figure 2. The regression of MAP over absolute interdialysis body weight gain also had a sigmoid distribution ($R^2 = 0.9118$; $P < 0.0001$). Body weight gain evolution during the year showed a cyclic pattern that paralleled rainfall records (Fig. 3), and both variables were also significantly correlated ($r = 0.659$; $P = 0.02$).

The evolution of blood pressure during the year similarly paralleled rainfall records (Fig. 3). There was a significant correlation between blood pressure and rainfall records ($r = 0.7863$; $P = 0.0024$ for systolic blood pressure, $r = 0.78405$; $P = 0.0025$ for diastolic blood pressure, $r = 0.79339$; $P = 0.0021$ for mean arterial pressure).

The annual evolution of minimal humidity followed that of the rainfall records. Thus, blood pressure and interdialytic body weight gain also had a parallel evolution with minimal humidity (Fig. 3). Correlations between minimal humidity and blood pressure were also significant ($r = 0.70163$; $P = 0.0110$ for systolic blood pressure, $r = 0.69957$; $P = 0.0113$ for diastolic blood pressure, $r = 0.70769$; $P = 0.01$ for mean arterial pressure, and $r = 0.5687$; $P = 0.0537$ for relative body weight gain). Daylight span was inversely correlated to SBP ($r = -0.7127$; $P < 0.01$) and DBP ($r = -0.6585$; $P < 0.02$).

The studies of maximal temperature showed some differences in regards to those of rainfall and humidity. Blood pressure and maximal temperature varied seasonally. However, the cycles of these variables were slightly shifted in regards to each other. Univariate correlation analyses between maximal temperature and blood pressure showed a strong correlation when the blood pressure values were correlated to the temperature of month + 2 ($r = -0.947$; $P < 0.0001$ and $r = -0.9308$; $P < 0.0001$ for systolic and diastolic blood pressure, $r = -0.9484$; $P < 0.0001$ for mean arterial pressure, and $r = -0.9285$; $P < 0.0001$ for interdialytic body weight gain), while there was no statistically significant correlation with the temperature of the month of observation (Fig. 4).

No correlation could be identified between atmospheric pressure and either blood pressure or body weight gain (data not shown).

Similar results were obtained when repeating the same analysis after exclusion of the 16 patients receiving antihypertensive drugs.

Multivariate stepwise regression analysis of systolic and diastolic blood pressure variations as dependent variables showed that body weight gain and rainfall were the only two variables retained in the model (Table 2).

DISCUSSION

In a longitudinally designed study over a four-year period, we previously reported a seasonal variation of blood pressure in hemodialysis patients, which was found to be related to climate factors [7]. The present study focused on the cycle of the year itself, regardless of time evolution, analyzing seven repeats of the annual cycle, more in a cross-sectional design, and with many more observations clarifies the blood pressure variations and suggests putative influencing factors. It shows that blood pressure variations are correlated to interdialytic body weight gain as well as to daylight span, rainfall, and humidity.

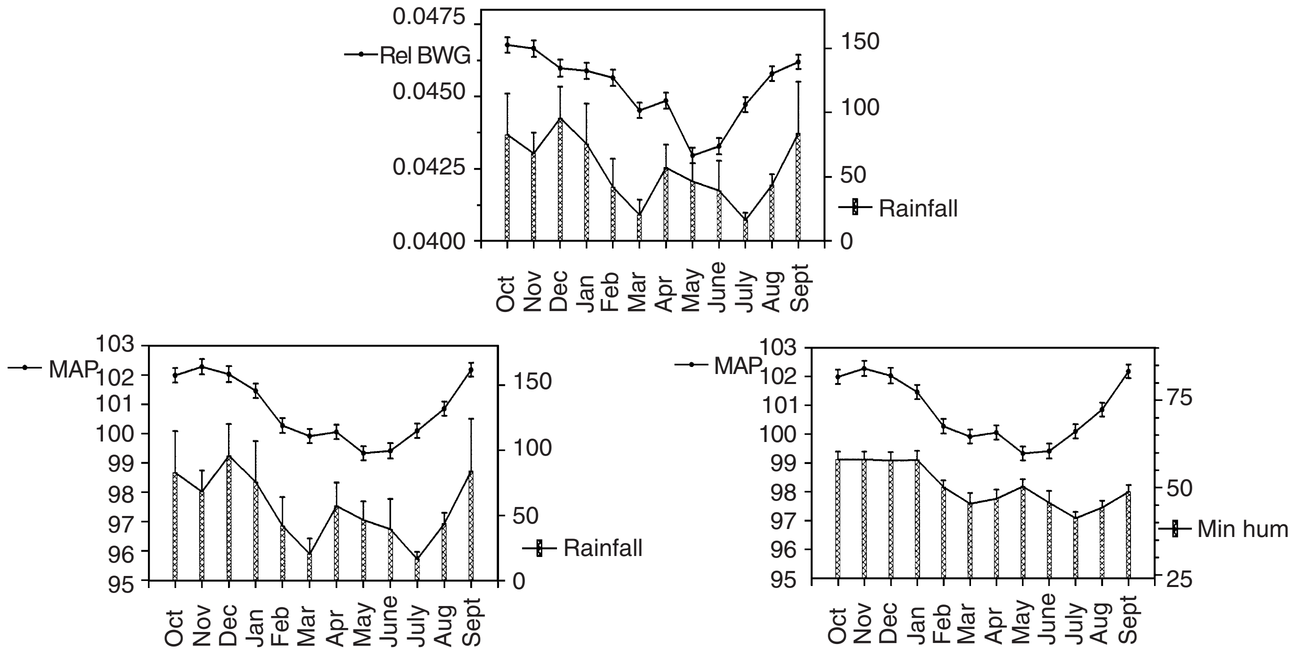

Fig. 3. Evolution of the relative body weight gain and mean arterial pressure along with the rainfall records and external humidity for the months of the year. Body weight gain between 2 dialyses (expressed in % of total body weight) follows the same pattern as that of rainfall records (in mm). Mean arterial pressure (mm Hg) follows the same pattern as that of rainfall and minimal humidity records. Body weight gain is significantly correlated to rainfall, and mean arterial pressure is significantly correlated to both rainfall and minimal humidity (see the **Results** section for details).

Following the design of the study, averaging each month of the year, for all the years at once, we expected to reduce the variability and the range of blood pressure values. At the same time, we expected to increase the sensitivity of the analysis by increasing the number of determinations per data point. Both the reduction in the variability and the increase in the reliability of the results were confirmed by the findings of the present study. Therefore, although the variation of systolic blood pressure in absolute terms was smaller than that we had observed in our previous longitudinal study [7], the present data are stronger and reinforce our initial findings, now with nearly double the number of patients and dialysis sessions included.

Our previous study [7] failed to show a parallel trend in the variations of blood pressure and of interdialytic body weight gain. This was certainly influenced by its longitudinal design. With the loss of residual renal function, which occurs over time in hemodialysis patients, we observed a gradual increase in the average interdialytic weight gain over the first two years, which might have perturbed our previous analysis. Our present data, short-cutting the bias of time, enabled us to identify the link between extracellular fluid overload and blood pressure, and we were able to establish that the equation defining this link was sigmoidal rather than linear (Fig. 2).

The results of our multivariate correlation studies retained interdialytic body weight gain as the first variable in the model, showing that interdialytic body weight gain (and probably its associated variations in extracellular volume status) greatly influences blood pressure level. Our univariate and multivariate correlation results complement the recent reports by Cheung et al [9], which identified body weight gain among the variables having a seasonal profile, and by Spósito et al [11], which showed an influence of daylight span on blood pressure.

A few longitudinal reports have described seasonal variations in blood pressure in nonrenal patients. Such a seasonal variation has been reported in hypertensive patients [2] and in normotensive subjects [12]. Large cross-sectional studies have also identified differences in blood pressure in normal subjects [1], as well as in hypertensive patients according to the time of the year it was measured [13]. Therefore, the seasonal pattern of blood pressure seems to include the general population, and it is particularly well observed in dialysis patients.

The sequence in the cycle of blood pressure seems to differ slightly from our previous analysis in that the maximum values and nadir of blood pressure preceded the extreme climate months (cold winter and hot summer). This pattern, which was already visible in some of the years included in our previous study [7], has been clearly confirmed by the present data and it is in keeping with the data reported by Spósito et al [11] from the southern hemisphere. These authors observed that the seasonal variation in blood pressure was inverse to that of the daylight span, rather than to the external temperature [11]. The months with extreme blood pressure values were,

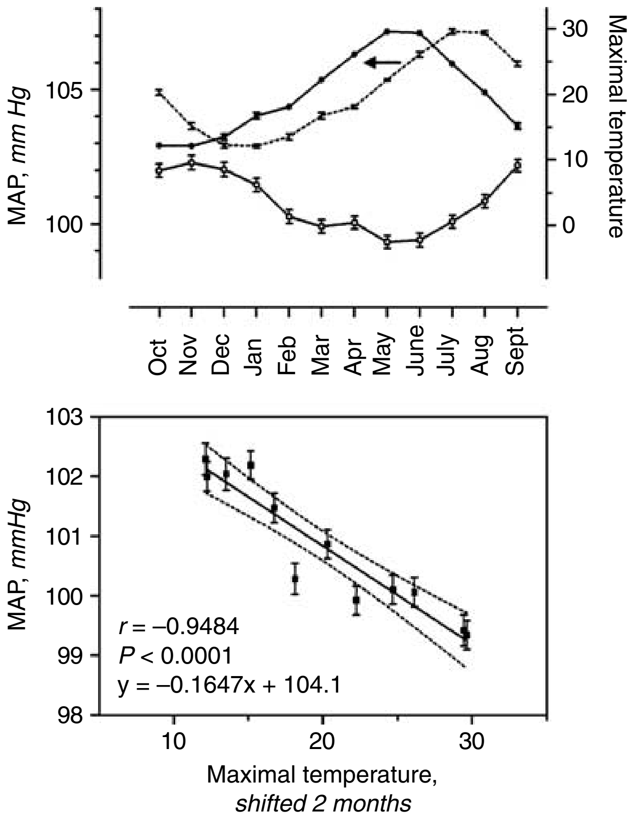

Fig. 4. Evolution of the mean arterial pressure along with maximal external temperature records for the months of the year and correlation studies. Mean arterial pressure (in mm Hg, bottom plots), as well as external temperature (top plot) as recorded (dashed line) and shifted by 2 months (solid lines), showing the opposite evolution of the clinical parameters preceding that of external temperature by 2 months. Corrected mean arterial pressure (–2 months) was significantly correlated to maximal temperature. The regression line equation is given.

Table 2. Multivariate stepwise regression analysis

Global analysis
Number of dialysis included = 38,769

Dependent variable	Model	Partial R^2	Model R^2	F value	P value
SBP					
1	IDBWG	0.8564	0.8564	59.65	<0.0001
2	Rainfall	0.0548	0.9112	3.14	0.0429
DBP					
1	IDBWG	0.7900	0.7900	37.62	0.0001
2	Rainfall	0.0692	0.8592	7.318	0.0647

Abbreviations are: SBP, systolic blood pressure; DBP, diastolic blood pressure; IDBWG, interdialytic body weight gain.

therefore, in late spring and late autumn, as we observed in our present data.

The mechanisms by which humidity and rainfall may interact with blood pressure are not clear. However, we can hypothesize that both volume state and peripheral resistance modifications may participate, the latter through variations in the vascular tone, and the former through variation in the loss of water by perspiration. In humid atmospheres the humidity gradient between the patient and the environment decreases, resulting in retention of part of the water volume that might have been lost by perspiration. This mechanism, which accounts for a small percentage of the total body weight in normal subjects, may have an increased relevance in the anuric state. However, the variations in volume state are not restricted to anuric patients. As commented by Parry et al [14], the increased incidence of heart failure in Nigerian women mimicking blood pressure variations may be a result of an increase in plasma volume [12].

Rostand [15] proposed parathyroid hormone (PTH) levels as a possible factor influencing blood pressure variations. An increase in the exposure to ultraviolet light from the sun results in an increase in photolysis of 7-dehydrocholesterol to pre-vitamin D3 and in vitamin D3 serum levels [16, 17], which in turn will decrease PTH synthesis [18]. Although we found no link between PTH serum levels and blood pressure [19], we have recently identified a correlation of blood pressure with vitamin D3 serum levels in the dialysis population [20], which has also been described in normal individuals [21]. These data are supportive of an effect for vitamin D3 and possibly of calcium metabolism on blood pressure control. Calcium metabolism may represent a mechanism establishing a link between the seasons of the year, sunlight exposure, and variations of blood pressure.

CONCLUSION

The present study clearly demonstrates that seasonal variations in blood pressure are related to interdialytic body weight gain changes (and most likely to the associated extracellular fluid modifications). It also shows that blood pressure and interdialytic body weight gain are correlated with climatic factors, such as daylight span, humidity, and rainfall. According to the present data, interdialytic body weight gain would be thought to be the main influencing factor on blood pressure variation in dialysis patients.

Reprint requests to Àngel Argilés, M.D., Ph.D., LGF–CNRS, 141, rue de la Cardonille, 34396 Montpellier Cedex 5, France.
E-mail: Angel.Argiles@igh.cnrs.fr

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